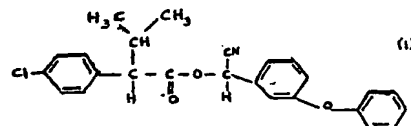


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C2C
(71) Applicant
Roussel Uclaf S.A.
35 Boulevard des
Invalides,
Paris 7^{ème}, France
(72) Inventors
Jacques Martel
Jean Tessier
Andre Teche
Jean-Pierre Demoute
(74) Agents
Frank B. Dehn & Co

(54) Optically-active substituted acetic acid derivatives

(57) Compounds of general formula I,



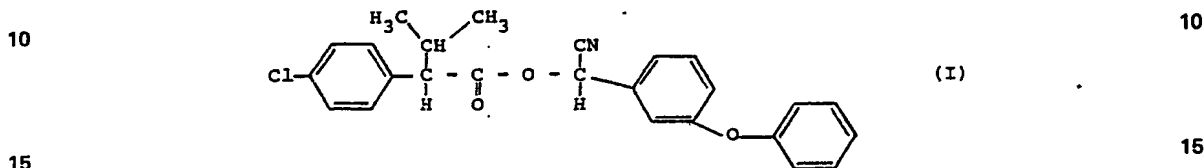
wherein the acidic residue is in either the D or L form, the alcoholic residue being in either racemic or optically-active form, which compounds possess an insecticidal activity clearly greater than the corresponding compounds of general formula I wherein the acidic residue is in the DL form.

SPECIFICATION

Optically-active substituted acetic acid derivatives

5 This invention relates to new esters of optically-active substituted acetic acid with racemic or optically-active substituted benzyl alcohol, to processes for their preparation and to insecticidal compositions containing them.

Compounds of general formula I



wherein the two asymmetric carbon atoms in the acidic residue are of racemic configuration are known. We have now found, however, that the compounds of general formula I which have been resolved into their D and L forms with respect to the acid residue, which have not previously been described, possess an insecticidal activity clearly greater than that of the corresponding hitherto known compounds which have not been resolved.

According to one feature of the present invention, therefore, there are provided compounds of general formula I as hereinbefore defined wherein the acidic residue is in either the "D" or "L" form, the alcoholic residue being in either racemic or optically-active form. Amongst these compounds of the invention, particular compounds which may be mentioned are:

(RS)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-*p*-chlorophenyl-acetate,
 (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate,
 (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate and
 (S)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-*p*-chlorophenyl-acetate.
 30 More preferred are the compounds of the invention in substantially pure form and especially the following:
 (RS)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-*p*-chlorophenyl-acetate having an $[\alpha]_D^{20}$ of + 6.1° at a concentration of 1% in ethanol,
 (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate having an $[\alpha]_D^{20}$ of -5° at a concentration of 1.2% in ethanol and
 35 crystalline (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate especially crystalline (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate having a melting point of 62°C and an $[\alpha]_D^{20}$ of + 13.15° at a concentration of 2% in benzene.

The compounds according to the invention may, for example, be prepared by reaction of α -cyano-3-phenoxybenzyl alcohol, in either (R), (S) or (RS) form, or a metallic or halogenated derivative thereof, with "L"- or "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid or a functional derivative thereof.
 40 The reaction is conveniently effected by reacting the α -cyano-3-phenoxybenzyl alcohol with "L"- or "D"-2-isopropyl-2-*p*-chlorophenyl-acetyl chloride, preferably in the presence of a tertiary base such as, for example, pyridine or triethylamine and preferably in the presence of an organic solvent such as benzene, toluene or methylene chloride. The acid chloride is conveniently formed by reaction of "L" or "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid with thionyl chloride.

Thus, according to one preferred embodiment, (RS)- α -cyano-3-phenoxybenzyl "D'-2-isopropyl-2-*p*-chlorophenyl-acetate may be obtained by reacting "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid with thionyl chloride in the presence of benzene and subsequently reacting the acid chloride thus obtained with (RS)- α -cyano-3-phenoxybenzyl alcohol in the presence of benzene and of pyridine:

50 According to a further preferred embodiment (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate may be obtained by reacting "D"-2-isopropyl-2-*p*-chlorophenyl acetic acid with thionyl chloride in the presence of benzene and subsequently reacting the acid chloride thus obtained with (S)- α -cyano-3-phenoxybenzyl alcohol in the presence of benzene and of pyridine:

Alternatively, if desired, the process for the preparation of the compounds of the invention may, for example, be effected by reacting the α -cyano-3-phenoxybenzyl alcohol with an anhydride or mixed anhydride of "L"- or "D"-2-isopropyl 2-*p*-chlorophenyl acetic acid, or a metallic derivative, e.g. an alkali metal derivative, of the α -cyano-3-phenoxybenzyl alcohol may be reacted with "L"- or "D"-2-isopropyl-2-*p*-chlorophenyl-acetyl chloride, or a halogenated derivative of the α -cyano-3-phenoxybenzyl alcohol may be reacted with an alkaline salt of "L"- or "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid. Methods for preparing halogenated and metallic derivatives of α -cyano-3-phenoxybenzyl alcohol as well as functional derivatives of "L"- or "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid are well known in the art.

"D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid, useful as a starting material in the above-described process for preparing compounds of the invention wherein the acidic residue is in the "D" form, may for example be obtained by acidic hydrolysis of the (-)- α -phenyl-ethylamine salt of "D"-2-isopropyl-2-*p*-chlorophenyl-acetic acid, which salt may itself be prepared, for example, by reaction of DL-2-isopropyl-2-*p*-chlorophenyl-acetic

acid with (-)- α -phenyl-ethylamine followed by crystallisation from aqueous ethanol, preferably 70% by volume aqueous ethanol.

"L"-2-isopropyl-2-*p*-chlorophenyl-acetic acid, also useful as a starting material to prepare compounds of the invention wherein the acidic residue is in the "L" form, may, for example be obtained by acidic hydrolysis of the (+)- α -phenyl-ethylamine salt of "L"-2-isopropyl-2-*p*-chlorophenyl-acetic acid, which salt may itself be prepared, for example, by reaction of DL-2-isopropyl-2-*p*-chlorophenyl-acetic acid with (+)- α -phenyl-ethylamine followed by crystallisation from aqueous ethanol, preferably 70% by volume aqueous ethanol.

"D"- and "L"-2-isopropyl-2-*p*-chlorophenyl-acetic acid, as well as the acid chlorides thereof, have not previously been described and thus, together with processes for their preparation, constitute a further feature of the present invention.

(S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate may also be prepared, if desired, by treating (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate with a basic agent in the presence of a solvent in which (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate is substantially insoluble and of an amount of (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate, e.g. obtained by the process described above, sufficient to initiate crystallisation of the (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate. The basic agent is preferably ammonia and the solvent is preferably isopropanol. The use of an initiator in the process is an important feature since without the initiator, crystallisation of the (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate does not occur. Hence this process only proved possible once the previously described process had been developed to provide the initiator.

Thus, as illustrated in Example 4 hereinafter, by use of an appropriate solvent such as e.g. isopropanol in which (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl acetate is substantially insoluble, and of a small sample of (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate, a solution of (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate when treated with ammonia yields a first fraction of (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate. Subsequent concentration of the mother liquors yields a residue consisting of a mixture of the (R) alcohol and (S) alcohol esters rich in the (R) alcohol ester. Treatment of this mixture with a base again in the presence of a solvent in which the (S) alcohol ester is substantially insoluble leads initially to a racemic mixture of the (RS) alcohol ester but the insolubility of the (S) alcohol ester in the solvent displaces the equilibrium whereby the (S) alcohol ester is obtained in a yield greater than 50%.

(S)- α -cyano-3-phenoxybenzyl alcohol may be prepared as described in our copending Application No 7903133 (corresponding to French Patent Application No 78-02621) of even date herewith. (R)- and (RS)- α -cyano-3-phenoxybenzyl alcohol are known from the literature.

As mentioned above, the compounds of general formula I according to the invention possess an interesting insecticidal activity clearly greater than that of the corresponding DL compounds and thus they are of use in the control of insects in the domestic and particularly the agricultural sphere. They permit effective control of, for example, aphides, the larvae of lepidoptera and coleoptera as well as flies and mosquitoes.

Thus, according to a still further feature of the present invention there are provided insecticidal compositions comprising, as active ingredient, at least one compound of formula I according to the invention in association with a carrier or excipient.

The compositions may, for example, be presented in the form of powders, granules, suspensions, emulsions, solutions, aerosols, combustible strips, baits or other preparations employed normally for the use of this kind of compound.

In addition to the active ingredient the compositions contain a carrier or excipient and optionally one or more other pesticidal agents and/or a non-ionic surface-active agent ensuring, in addition, uniform dispersion of the substances constituting the mixture. The carrier or excipient used may be a liquid such as e.g. water, an alcohol, a hydrocarbon or another organic solvent, a mineral, animal or vegetable oil, or a powder such as e.g. talc, a clay, a silicate, Kieseluhr or a combustible solid such as tabu powder (or pyrethrum marc).

To increase the insecticidal activity of the compositions a synergist may be included, for example one of the synergists known for use in such a case such as e.g. 1-(2,5,8-trioxadodecyl-2-propyl-4,5-methylenedioxy)-benzene (piperonyl butoxide), N-(2-ethylheptyl)-bicyclo (2,2,1) hept-5-ene-2,3-dicarboximide or piperonyl-bis-2-(2'-n-butoxy-ethoxy)-ethyl acetal (tropital).

The insecticidal compositions according to the invention preferably contain from 0.005% to 10% by weight of active ingredient. According to a still further feature of the present invention there is provided a method of preventing or inhibiting the growth and/or proliferation of insects which comprises administering to a site infested with or susceptible to infestation with insects an effective amount of a compound of formula I according to the invention.

The following non-limiting examples serve to illustrate the present invention.

Example 1: Ester of (R,S.) α -cyano 3-phenoxy benzyl alcohol of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

Stage A: Salt of (+) α -phenyl ethyl amine of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

Into 4 litres of ethanol containing 70% of water (by volume) one introduces 250 g of DL 2-isopropyl

2-parachloro-phenyl acetic acid, one agitates, adds to the solution obtained 140 g of (+) α -phenyl ethyl amine, observes precipitation, heats to reflux the reaction mixture, adds alcohol containing 70% of water (by volume) until total dissolution, allows to cool gently, observes a beginning of crystallisation at about 65°C, agitates at 20°C for 48 hours, isolates by vacuum-filtration the precipitate formed, washes it with ethanol and obtains 188.9 g of crude salt of (+) α -phenyl ethyl amine of "L" 2-isopropyl 2-parachlorophenyl acetic acid. $[\alpha]_D^{20} = +3.5^\circ$ ($c = 0.5\%$ methanol).

Purification:

The 188.9 g of crude product are introduced into 4 litres of ethanol containing 70% of water (by volume), one heats to reflux, adds ethanol containing 70% of water (by volume) to obtain total dissolution (say 2 litres), allows to cool to 20°C, agitates for 20 hours at 20°C, isolates by vacuum-filtration the precipitate formed, washes it, dries it and obtains 147.9 g of salt of (+) α -phenyl ethyl amine of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = +4.5^\circ$ ($c = 0.8\%$ ethanol) $F = 210^\circ\text{C}$ (with decomposition).

Stage B: "L" 2-isopropyl 2-parachlorophenyl acetic acid.

Into 300 cm³ of methylene chloride one introduces 147.5 g of salt of (+) α -phenyl ethyl amine of "L" 2-isopropyl 2-parachlorophenyl acetic acid obtained in Stage A, one adds under agitation 300 cm³ of 2 N aqueous solution of hydrochloric acid, agitates for 15 minutes, obtains two clear phases, separates them by decanting, extracts the aqueous phases with methylene chloride, washes the organic phases with water, extracts the washing waters with methylene chloride, dries the organic phase, filters, concentrates to dryness and obtains 94 g of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = -41.5^\circ$ ($c = 0.9\%$ ethanol) M.Pt. = 105°C.

25 Circular dichroism (dioxan)

$\Delta\epsilon = -4$ at 218 nm (max), $\Delta\epsilon = +0.029$ at 251 nm (max)
 $\Delta\epsilon = +0.011$ at 259 nm (max), $\Delta\epsilon = -0.011$ at 263 nm (max)
 $\Delta\epsilon = +0.021$ at 267 nm (max), $\Delta\epsilon = -0.018$ at 271 nm (max)
 $\Delta\epsilon = +0.04$ at 275 nm (max), $\Delta\epsilon = -0.008$ at 278 nm (max)

Stage C: Chloride of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

One agitates at reflux, for 4 hours, a mixture constituted by 10 g of "L" 2-isopropyl 2-parachlorophenyl acetic acid (obtained in Stage B), 50 ml of petroleum ether and 20 ml of thionyl chloride, concentrates to dryness by distillation under reduced pressure and obtains 10.8 g of acid chloride which one uses in benzene solution in Stage D of the present Example.

Stage D: Ester of (R,S) α -cyano 3-phenoxy benzyl alcohol of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

Into a mixture of 10 cm³ of benzene and of 5 cm³ of pyridine one introduces 5.5 g of (R,S) α -cyano 3-phenoxy benzyl alcohol, then over 15 minutes at 20°C 25 cm³ of a benzene solution of chloride of "L" 2-isopropyl 2-parachlorophenyl acetic acid, titrating 24 g per 100 cm³ (corresponding to 6 g of acid), agitates at 20°C for 15 hours, adds water, agitates, separates by decanting the aqueous phase, extracts it with benzene, washes the organic phase with water, extracts the washing waters with benzene, dries the benzene solution, filters, concentrates to dryness by distillation under reduced pressure, chromatographs the residue on silica gel eluting with a mixture of cyclohexane and of acetone ((95:5) then of cyclohexane and of ethyl acetate (95:5) and obtains 6.93 g of ester of (R,S) α -cyano 3-phenoxy benzyl alcohol of "L" 2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = +6.1^\circ$ ($c = 1\%$, ethanol)

Analysis : C₂₅ H₂₂ O₃ NCl (419.88)

	C%	H%	N%	Cl%
Calculated:	71.51	5.28	3.33	8.44
Found:	71.6	5.3	3.2	8.5

Ultra-violet spectrum (ethanol)

Inflection at 225 nm ($E_1^1 = 520$), maximum at 267 nm ($E_1^1 = 48$) maximum at 271 nm ($E_1^1 = 50$), maximum at 277 nm ($E_1^1 = 52$); Inflection at 284 nm ($E_1^1 = 36$); inflection at 305 nm ($E_1^1 = 1.5$).

Circular dichroism (dioxan)

$\Delta\epsilon = +0.13$ at 280 nm (maximum); $\Delta\epsilon = +0.17$ at 274 nm
 $\Delta\epsilon = +0.11$ at 267 nm (maximum); $\Delta\epsilon = 0.07$ at 260 nm (max)
 $\Delta\epsilon = +6.25$ at 227 nm (maximum).

NMR Spectrum (deutero chloroform)

Peaks at 0.65 - 0.76 p.p.m.; 0.67 - 0.78 p.p.m.; 0.9 - 1.0 p.p.m.; 1.0 - 1.12 p.p.m. characteristic of the methyls of the isopropyl.

Peaks at 2.0 - 2.67 p.p.m.; characteristic of the hydrogen of the isopropyl situated at α of the asymmetric carbon.

Peaks at 3.15 - 3.32 p.p.m.; characteristic of the hydrogen borne by the asymmetric carbon of the acid.

Peaks at 6.32 - 6.35 p.p.m.; characteristic of the hydrogen borne by the same carbon as the nitrile group.

5 Peaks at 6.83 - 7.58 p.p.m; characteristic of the hydrogens of the aromatic nuclei.

Example 2; Ester (R,S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid.

Stage A: Recovery of the mixture of "D" 2-isopropyl 2-parachlorophenyl acetic acid and of "DL" 2-isopropyl 2-parachlorophenyl acetic acid.

One concentrates to dryness the mother liquors of resolution and of purification previously obtained in
10 Example 1, puts the residue obtained into suspension in 300 cm³ of methylene chloride, adds under agitation a 2 N aqueous solution of hydrochloric acid until pH = 1 (say about 350 cm³ of 2 N solution), agitates, separates by decanting the organic phase, extracts the aqueous phase with methylene chloride, combines the organic phases, washes them with water, extracts the washing waters with methylene chloride, dries the organic phase, filters, concentrates to dryness by distillation under reduced pressure and obtains 153.5 g of a
15 mixture of "D" 2-isopropyl 2-parachlorophenyl acetic acid and of "DL" 2-isopropyl 2-parachlorophenyl acetic acid.

Stage B: Salt of (-) α -phenyl ethyl amine of "D" 2-isopropyl 2-parachlorophenyl acetic acid.

Into 4 litres of ethanol containing 70% of water (by volume) one introduces 153 g of mixture of "D"
20 2-isopropyl 2-parachlorophenyl acetic acid and of "DL" 2-isopropyl 2-parachlorophenyl acetic acid, adds to the solution obtained, over 15 minutes, 86 g of (-) α -phenyl ethyl amine, takes the mixture to reflux under agitation, adds ethanol containing 70% of water (by volume) until total dissolution (2.25 litres), allows to cool slowly, agitates for 20 hours at 20°C, isolates and vacuum-filters the precipitate formed, washes it with ethanol, dries it and obtains 168.2 g of crude salt of (-) α -phenyl ethyl amine of "D" 2-isopropyl
25 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = -5^\circ (c = 0.6\%, \text{methanol})$

Purification:

Into 4 litres of aqueous solution of ethanol containing 70% of water (by volume) one introduces 168 g of
30 crude salts of (-) α -phenyl ethyl amine of "D" 2-isopropyl 2-parachlorophenyl acetic acid, takes the mixture to reflux, adds ethanol containing 70% of water (by volume) until total dissolution is obtained (1.5 litres), allows to cool to 20°C, agitates at 20°C for 48 hours, isolates by vacuum-filtration the precipitate formed, washes it with ethanol, dries it and obtains 143.1 g of salt of (-) α -phenyl ethyl amine of "D" 2-isopropyl
35 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = -5^\circ (c = 0.8\% \text{ methanol, M.Pt.} = 210^\circ\text{C (with decomposition)})$

Stage C: "D" 2-isopropyl 2-parachlorophenyl acetic acid.

Using a modus operandi similar to that of Stage B of Example 1, starting with 143 g of salt of (-) α -phenyl
40 ethyl amine of "D" 2-isopropyl 2-parachlorophenyl acetic acid obtained in Stage B of Example 2, one obtains 91 g of "D" 2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = +42^\circ (c = 1\%, \text{ethanol}), \text{M.Pt.} = 105^\circ\text{C.}$

Stage D: Chloride of "D" 2-isopropyl 2-parachlorophenyl acetic acid.

45 Into a mixture of 50 cm³ of petroleum ether (B.Pt. 35-70°) and of 20 cm³ of thionyl chloride one introduces 10 g of "D" 2-isopropyl 2-parachlorophenyl acetic acid, one takes the mixture to reflux, maintains it there for 4 hours, cools, concentrates to dryness under reduced pressure and obtains 10.8 g of chloride of "D"
2-isopropyl 2-parachlorophenyl acetic acid.

50 *Stage E: Ester of (R,S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid.*

Into a mixture of 10 cm³ of benzene and of 5 cm³ of pyridine one introduces 5.5 g of (R,S) α -cyano
3-phenoxy benzyl alcohol, then at 20 °C g of chloride of "D" 2-isopropyl 2-parachlorophenyl acetic acid in solution in 20 cm³ of benzene, one agitates at 20°C for 15 hours, adds water, agitates, allows to stand,
55 decants, extracts the aqueous phase with benzene, washes the organic phase with water, extracts the washing waters with benzene, dries the benzene solution, filters, concentrates to dryness by distillation under reduced pressure, chromatographs the residue on silica gel eluting with a mixture of cyclohexane and
of ethyl acetate (95:5) and obtains 8.57 g of ester of (R,S) α -cyano 3-phenoxy benzyl alcohol of "D"
2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = -5^\circ (c = 1.2\% \text{ ethanol})$

60 *Analysis* : C₂₅ H₂₂ O₃ NCl - (419.88)

C% H% N% Cl%

Calculated: 71.51 5.28 3.33 8.44

Found: 71.5 5.3 3.3 8.6

Ultra-violet spectrum (ethanol)

Inflection at 225 nm ($E_1^1 = 534$), $\epsilon = 22400$, inflection at 260 nm ($E_1^1 = 36$) Inflection at 269 nm ($E_1^1 = 48$),
inflection at 272
nm ($E_1^1 = 50$) Maximum at 278 nm ($E_1^1 = 54$), $\epsilon = 2200$, inflection at 283 nm ($E_1^1 = 40$)

5

Circular dichroism (dioxan)

$\Delta\epsilon = -0.13$ at 282 nm (max); $\Delta\epsilon = -0.17$ at 274 nm (max)
 $\Delta\epsilon = -0.12$ at 267 nm (max); $\Delta\epsilon = -0.08$ at 258 nm (max)
 $\Delta\epsilon = -6.78$ at 228 nm (max).

10

NMR Spectrum (deutero chloroform)

Peaks at 0.62 - 0.73 p.p.m., 0.63 - 0.75 p.p.m., 0.88 - 0.98 p.p.m.

Peaks at 0.98 - 1.05 p.p.m., characteristic of the methyls of the isopropyl.

Peaks at 1.92 - 2.66 p.p.m., characteristic of the hydrogen of the isopropyl situated at α of the asymmetric

15

carbon.
Peaks at 3.16 - 3.33 p.p.m., characteristic of the hydrogen borne by the asymmetric carbon of the acid.

Peaks at 6.32 - 6.36 p.p.m., characteristic of the hydrogen borne by the same carbon as the nitrile group.

Peaks at 6.83 - 7.58 p.p.m., characteristic of the hydrogens of aromatic nuclei.

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Example 3: Ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid.

Into 50 cm³ of benzene one introduces 3 g of (S) α -cyano 3-phenoxy benzyl alcohol and 3.1 g of chloride of
"D" 2-isopropyl 2-parachlorophenyl acetic acid obtained as in Stage D of Example 2, one cools to +15°C,
introduces, drop by drop, a mixture of 4 cm³ of pyridine and of 10 cm³ of benzene, agitates for 2 hours at
20°C, pours on to a 2 N aqueous solution of hydrochloric acid, separates by decanting the organic phase,

25

dries it, filters, concentrates to dryness by distillation under reduced pressure, chromatographs the residue
on silica gel eluting with benzene and obtains 4.4 g of ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D"
2-isopropyl 2-parachlorophenyl acetic acid.

$[\alpha]_D^{20} = +13.15^\circ$ ($c = 2\%$, benzene). This product crystallises out. M.Pt. = 62°C.

Analysis : C₂₅ H₂₂ Cl NO₃ (419.88)

30

C% H% Cl% N%

Calculated: 71.50 5.28 8.44 3.34

Found: 71.4 5.3 9.1 3.3

Circular dichroism (dioxan)

$\Delta\epsilon = +0.1$ at 253 nm (max), $\Delta\epsilon = +0.23$ at 277 nm (max),

35

$\Delta\epsilon = +0.27$ at 282 nm (max), $\Delta\epsilon = +0.27$ at 286 nm (max).

NMR Spectrum (deutero chloroform)

Peaks at 0.63 - 0.75 p.p.m., 0.88 - 1.0 p.p.m., characteristic of the hydrogens of the methyls of the isopropyl.

Peaks at 2.25 p.p.m., characteristic of the hydrogen of the isopropyl borne by the carbon at α of the
asymmetric carbon. Peaks at 3.17 - 3.33 p.p.m., characteristic of the hydrogen borne by the asymmetric

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carbon of the acid.

Peaks at 6.4 p.p.m., characteristic of the hydrogen borne by the carbon at α of the nitrile group.

Peaks at 6.91 - 7.58 p.p.m., characteristic of the hydrogens of the aromatic nuclei.

The (S) α -cyano 3-phenoxy benzyl alcohol can be prepared in the following manner:

45

Stage A: Mixture of (1R,5S) 6,6-dimethyl 4(R) [(S)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0] hexan-2-one and of (1R,5S) 6,6-dimethyl 4(R). [(R)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0] hexan-2-one.

One mixes 22.5 g of (R,S) α -cyano 3-phenoxy benzyl alcohol, 9.46 g of lactone of *cis* 2,2-dimethyl 3
S-(dihydroxy-methyl) cyclopropane-1R-carboxylic acid and 0.150 g of monohydrated paratoluene sulphonic
acid, takes to 80°C under a vacuum of 10⁻² mm of mercury and maintains the reaction mixture of 2 hours
under these conditions, the water formed being removed by distillation. One cools to 20°C and obtains 30.70
g of crude mixture of (1R,5S) 6,6-dimethyl 4(R) [(S)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0]
hexan-2-one and of (1R,5S) 6,6-dimethyl 4(R) [(R)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0]
hexan-2-one (containing as impurities mainly the starting products which have not reacted). (Mixture A).

55

Stage B: [1R, 5S] 6,6-dimethyl 4(R) [(S)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0] hexan-2-one.

One chromatographs the mixture A obtained in Stage A on silica gel eluting with a mixture of benzene and
ethyl acetate (95:5) and obtains 10.9 g of [1R,5S] 6,6-dimethyl 4(R) [(R) [(S)-cyano (3'-phenoxyphenyl)
methoxy] 3-oxabicyclo [3.1.0] hexan-2-one.

60

M.Pt = 126°; $[\alpha]_D^{20} = -71^\circ$ ($c = 1\%$, benzene)

Ultra-violet spectrum (ethanol)

Inflection at 226 nm ($E_1^1 = 319$); inflection at 267 nm ($E_1^1 = 52$);

Inflection at 271 nm ($E_1^1 = 56$); maximum at 276 nm ($E_1^1 = 60$);

65

Inflection at 280 nm ($E_1^1 = 46$).

Circular dichroism (dioxan) $\Delta\epsilon = -4.2$ at 225 nm (max) $\Delta\epsilon = +0.39$ at 287 nm (max).*NMR Spectrum* (deuteriochloroform)

- 5 Peaks at 1.18 - 1.23 p.p.m., characteristic of the hydrogens of the geminal methyls. 5
 Peaks at 1.98 - 2.08 and 2.15 - 2.25 p.p.m., characteristic of the hydrogens of the isopropyls ;
 Peaks at 5.53 - 5.54 p.p.m., characteristic of the hydrogen borne by the same carbon as the nitrile group and of the hydrogen at position 4.

Stage C: (S) α -cyano 3-phenoxy benzyl alcohol

- 10 Into a mixture of 100 cm³ of dioxan and 50 cm³ of water one introduces 10 g of (1R,5S) 6,6 dimethyl 4 (R) 10
 [(S)-cyano (3'-phenoxyphenyl) methoxy] 3-oxabicyclo [3.1.0] hexan-2- one, obtained in Stage B above, then
 1 g of mono-hydrated paratoluene sulphonic acid, one takes the reaction mixture to reflux, maintains it there
 for 23 hours, concentrates by distillation under reduced pressure until half of the initial volume is obtained,
 adds ethyl ether, agitates, separates by decanting the organic phase, wuyhes it with water, dries it, concen-
 15 trates it to dryness by distillation under reduced pressure, chromatographs the residue (9.5 g) on silica gel 15
 eluting with a mixture of benzene and of ethyl acetate (9:1) and obtains 6.1 g of (S) α -cyano 3-phenoxy
 benzyl alcohol.

 $[\alpha]^{20}_D = -16.5 \pm 1.5$ ($c = 0.8\%$ benzene).*NMR Spectrum* (deuteriochloroform)

- 20 Peaks at 3.25 p.p.m., characteristic of the hydrogen of the alcohol function. 20
 Peaks at 5.41 p.p.m., characteristic of the hydrogen borne by the same carbon as the nitrile group.
Example 4: Ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid.
 Into a mixture of 60 cm³ of isopropanol and 2 cm³ of triethylamine one introduces 31.5 g of ester of
 (R,S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-para chlorophenyl acetic acid, one agitates for
 25 24 hours at 20°C, then for 24 hours at 0°C, initiates crystallisation by the addition of a small amount of ester 25
 of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachloro phenyl acetic acid (crystalline, M.Pt.
 = 62°C), agitates for 24 hours at 0°C, then for 48 hours at -10°C, isolates by vacuum-filtration the precipitate
 formed, dries it and obtains 6.1 g of first yield, M.Pt. = 62°C. One concentrates the mother liquors to dryness
 by distillation under reduced pressure, adds to the residue 60 cm³ of petroleum ether (B.P.t. = 35-75°C) and
 30 10 cm³ of isopropanol, adds 2 cm³ of 22°Bé concentrated aqueous solution of ammonia, agitates for 72 hours 30
 at -10°C, isolates by vacuum-filtration the precipitate formed, washes it, dries it and obtains 13.5 g of second
 * yield (M.Pt. = 62°C).

- The two yields obtained above are combined and crystallised from isopropanol. One obtains 17.9 g of
 ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid, M.Pt. =
 35 62°C. 35

Example 5: Insecticidal compositions.

- One prepared an insecticidal composition in the form of emulsifiable concentrate by mixing homogen-
 40 ously: 40
 -Ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic.
 acid0.3 g
 -Piperonyl butoxide0.5 g
 45 -Topanol A0.1 g 45
 -Xylene99.1 g

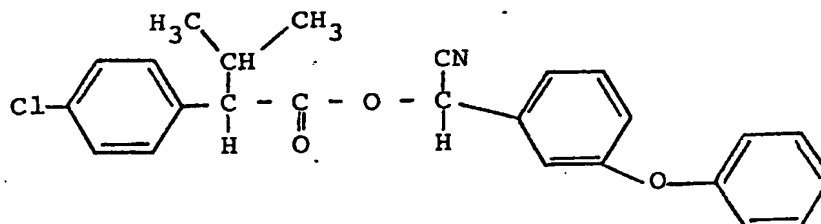
Example 6: Smoke-producing composition

- 50 One mixes homogeneously: 50
 -Ester of (S) α -cyano 3-phenoxy benzyl alcohol of "D" 2-isopropyl 2-parachlorophenyl acetic acid1g
 -Tabu powder25 g
 -Cedar-needle powder39.25g
 55 -Pine-wood powder33.75 g 55
 -Bright green0.5 g
 -p-nitro phenol0.5 g

60 CLAIMS

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1. Compounds of general formula I,



wherein the acidic residue is in either the "D" or "L" form, the alcoholic residue being in either racemic or optically active form.

2. (RS)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-p-chlorophenyl-acetate.
3. (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-p-chlorophenyl-acetate.
- 5 4. (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-p-chlorophenyl-acetate.
- 5 5. (S)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-p-chlorophenyl-acetate.
6. Compounds as claimed in any preceding claim in substantially pure form.
7. (RS)- α -cyano-3-phenoxybenzyl "L"-2-isopropyl-2-p-chlorophenyl-acetate having an $[\alpha]_{20/D}$ of $+6.1^\circ$ at a concentration of 1% in ethanol.
- 10 8. (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-p-chlorophenyl-acetate having an $[\alpha]_{20/D}$ of $+6.1^\circ$ at a concentration of 1.2% in ethanol.
9. Crystalline (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-p-chlorophenyl-acetate.
10. Crystalline (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-p-chlorophenyl-acetate having a melting point of 62°C and an $[\alpha]_{20/D}$ of $+13.15^\circ$ at a concentration of 2% in benzene.
- 15 11. A process for the preparation of compounds of general formula I as claimed in claim 1 which comprises reacting α -cyano-3-phenoxybenzyl alcohol in either (R), (S) or (RS) form, or a metallic or halogenated derivative thereof, with "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetic acid or a functional derivative thereof.
12. A process as claimed in claim 11 wherein the α -cyano-3-phenoxybenzyl alcohol is reacted with "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetate chloride.
- 20 13. A process as claimed in claim 12 wherein the reaction is effected in the presence of a tertiary base.
14. A process as claimed in claim 12 wherein or claim 13 wherein the reaction is effected in the presence of benzene, toluene or methylene chloride as solvent.
15. A process as claimed in any one of claims 12 to 14 wherein the "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetyl chloride is obtained by reaction of "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetic acid with thionyl chloride.
- 25 16. A process as claimed in claim 15 for the preparation of (RS)- α -cyano-3-phenoxybenzyl "D"-isopropyl-2-p-chlorophenyl-acetic acid with thionyl chloride in the presence of benzene and subsequently reacting the acid chloride thus obtained with (RS)- α -cyano-3-phenoxybenzyl 1 alcohol in the presence of benzene and of pyridine.
- 30 17. A process as claimed in claim 15 for the preparation of (S)- α -cyano-3-phenoxybenzyl "D"-isopropyl-2-p-chlorophenyl-acetate which comprises reacting "D"-2-isopropyl-2-p-chlorophenyl-acetyl chloride with (S)- α -cyano-3-phenoxybenzyl alcohol in the presence of benzene and of pyridine.
- 35 18. A process as claimed in claim 11 wherein the α -cyano-3-phenoxybenzyl alcohol is reacted with an anhydride or mixed anhydride of "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetic acid.
19. A process as claimed in claim 11 wherein an alkali metal derivative of the α -cyano-3-phenoxybenzyl alcohol is reacted with "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetyl chloride.
20. A process as claimed in claim 11 wherein a halogenated derivative as claimed in claim 11 wherein a halogenated derivative of the α -cyano-3-phenoxybenzyl alcohol is reacted with an alkaline salt of the "L" or "D"-2-isopropyl-2-p-chlorophenyl-acetic acid.
- 40 21. A process as claimed in any one of claims 11 to 20, for the preparation of a compound of formula I wherein the acidic residue is in the "D" form, wherein the "D"-2-isopropyl-2-p-chlorophenyl-acetic acid is obtained by acidic hydrolysis of the (-)- α -phenyl-ethylamine salt of "D"-2-isopropyl-2-p-chlorophenyl-acetic acid.
- 45 22. A process as claimed in claim 21 wherein the (-)- α -phenyl-ethylamine salt of "D"-2-isopropyl-2-p-chlorophenyl-acetic acid is obtained by reaction of DL-2-isopropyl-2-p-chlorophenyl-acetic acid with (-)- α -phenyl-ethylamine followed by crystallisation from aqueous ethanol.
23. A process as claimed in any one of claims 11 to 15 and 18 to 20, for the preparation of a compound of formula I wherein the acidic residue is in the "L" form, wherein the "L"-2-isopropyl-2-p-chlorophenyl-acetic acid is obtained by acidic hydrolysis of the (+)- α -phenyl-ethylamine salt of "L"-2-isopropyl-2-p-chlorophenyl-acetic acid.
- 50 24. A process as claimed in claim 23 wherein the (+)- α -phenyl-ethylamine salt of "L"-2-isopropyl-2-p-chlorophenyl-acetic acid is obtained by reaction of DL-2-isopropyl-2-p-chlorophenyl-acetic acid with (+)- α -phenyl-ethylamine followed by crystallisation from aqueous ethanol.
- 55

25. A process for the preparation of (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate which comprises treating (RS)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate with a basic agent in the presence of a solvent in which (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate is substantially insoluble and of an amount of (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate sufficient to initiate crystallisation of the (S)- α -3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate. 5
26. A process as claimed in claim 25 wherein the (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate added to initiate crystallisation is obtained by a process as claimed in any one of claims 11 to 22.
- 10 27. A process as claimed in claim 25 or claim 26 wherein the basic agent is ammonia. 10
28. A process as claimed in any one of claims 25 to 27 wherein the solvent is isopropanol.
29. A process for the preparation of compounds of general formula I as claimed in claim 1 substantially as herein described.
30. A process for the preparation of compounds of general formula I as claimed in claim 1 substantially as herein described in any one of Examples 1 to 4. 15
31. Compounds of general formula I as claimed in claim 1 whenever prepared by a process as claimed in any one of claims 11 to 30.
32. Insecticidal compositions comprising, as active ingredient, at least one compound as claimed in claim 1 in association with a carrier or excipient.
- 20 33. Compositions as claimed in claim 32 wherein the active ingredient comprises (S)- α -cyano-3-phenoxybenzyl "D"-2-isopropyl-2-*p*-chlorophenyl-acetate. 20
34. Compositions as claimed in claim 32 wherein the active ingredient comprises a compound as claimed in any one of claims 2, 3 and 5 to 10.
35. Compositions as claimed in any one of claims 32 to 34 further including one or more other pesticidal agents. 25
36. Compositions as claimed in any one of claims 32 to 35 further including a non-ionic surface-active agent.
37. Compositions as claimed in any one of claims 32 to 36 in the form of powders, granules, suspensions, emulsions, solutions, aerosols, combustible strips or baits.
- 30 38. Compositions as claimed in any one of claims 32 to 37 further including a synergist. 30
39. Compositions as claimed in claim 38 wherein the synergist is 1-(2,5,8-trioxa-dodecyl-2-propyl-4,5-methylene dioxy)-benzene, N-(2-ethylheptyl)-bicyclo[2,2,1]-hept-5-ene-2,3-dicarboximide or piperonyl-bis-2-(2'-*n*-butoxy-ethoxy)-ethyl acetal.
40. Compositions as claimed in any one of claims 32 to 39 containing from 0.005 to 10% by weight of active ingredient. 35
41. Compositions as claimed in claim 32 substantially as herein described.
42. Compositions substantially as herein described in Example 5 or Example 6.
43. A method of preventing or inhibiting the growth and/or proliferation of insects which comprises administering to a site infested with or susceptible to infestation with insects an effective amount of a compound of formula I as claimed in claim 1. 40
44. "D"- and "L"-2-isopropyl-2-*p*-chlorophenyl-acetic acids and the acid chlorides thereof.
45. A process for the preparation of compounds as claimed in claim 44 substantially as herein described.
46. Each and every novel method, process, compound and composition herein disclosed.